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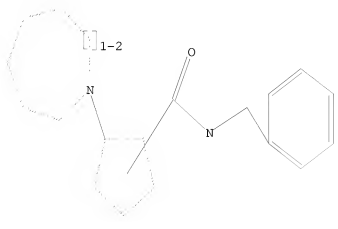


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Structure attributes must be viewed using STN Express query preparation.

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L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:99600 CAPLUS
DOCUMENT NUMBER: 142:198060
TITLE: Preparation of 7 and 8 membered heterocyclic cyclopentyl benzylamide derivatives as modulators of chemokine receptor activity
INVENTOR(S): Ge, Min; Goble, Stephen D.; Pasternak, Alexander; Yang, Lihu
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005010154	A2	20050203	WO 2004-US21996	20040709
WO 2005010154	A3	20050825		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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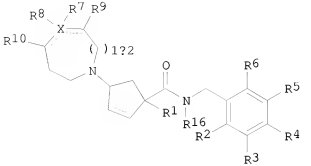
CA 2532102	A1	20050203	CA 2004-2532102	20040709
EP 1646392	A2	20060419	EP 2004-777832	20040709
CN 1871012	A	20061129	CN 2004-80020467	20040709
JP 2007523871	T	20070823	JP 2006-520232	20040709
IN 2005DN06171	A	20080509	IN 2005-DN6171	20051230
US 20060183731	A1	20060817	US 2006-564702	20060113
PRIORITY APPLN. INFO.:			US 2003-487317P P	20030715
			WO 2004-US21996 W	20040709

OTHER SOURCE(S): CASREACT 142:198060; MARPAT 142:198060
GI



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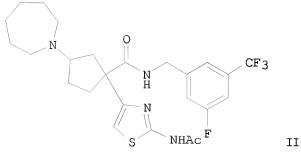


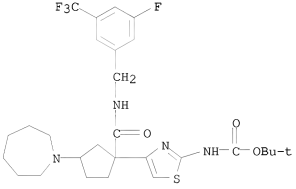
II

AB N-benzylheterocyclylcyclopentanecarboxamide derivs. of the formula (I) and pharmaceutically acceptable salts thereof and individual diastereomers thereof [X = O, N, S, SO2, C; R1 = H, C1-6 alkyl, -C0-6alkyl-O-C1-6alkyl, -C0-6 alkyl-S-C1-6-alkyl, - (C0-6-alkyl)(C3-7cycloalkyl)(C0-6alkyl), HO, heterocyclyl, cyano, etc.; R2, R4, R6 = H, each (un)substituted C1-3 alkyl or -O-C1-3alkyl, HO, Cl, F, Br, Ph; R3 = H, HO, halo, each (un)substituted C1-3 alkyl or NH2, etc.; R5 = each (un)substituted C1-6 alkyl, -O-C1-6alkyl, -CO-C1-6alkyl, -S-C1-6alkyl, or 1-pyridyl, F, Cl, Br, (un)substituted -C4-6 cycloalkyl, etc.; R7 = H, (C0-6-alkyl)phenyl, (C0-6alkyl)heterocycle, (C0-6-alkyl)-C3-7cycloalkyl, etc.; R8 = H, nothing (when X is either O, S, SO2, or N or when a double bond joins the carbons to which R7 and R10 are attached), HO, C1-6 alkyl, C1-6-alkylhydroxy, -O-C1-3alkyl, (un)substituted CONH2, cyano; or where R7 and R8 may be joined together to form a ring such as 1H-indene, 2,3-dihydro-1H-indene, etc.; or R7 and R9 or R8 and R10 may be joined together to form an (un)substituted Ph or heterocycle ring; R9, R10 = H, HO, hydroxy, C1-6 alkyl, C1-6 alkylhydroxy, -O-C1-3alkyl, oxo (when R9 or R10 is connected to the ring via a double bond), halo, etc.; R16 = H, Ph, (un)substituted C1-6alkyl; the dashed line represents a single or a double bond] are prepared These compds. are useful as modulators of chemokine receptor, in particular chemokine receptor CCR-2, for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease, in particular rheumatoid arthritis. Thus, reductive amination of 1-[2-[N-(tert-butoxycarbonyl)amino]thiazol-4-yl]-3-oxocyclopentane-1-carboxylic acid Et ester by hexamethyleneimine and NaBH(OAc)2 in THF followed by alkali hydrolysis and acidification with AcOH gave 3-(Azepan-1-yl)-1-[2-[N-(tert-butoxycarbonyl)amino]thiazol-4-yl]cyclopentane-1-carboxylic acid which underwent amidation with 3-fluoro-5-(trifluoromethyl)benzylamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in the presence of 4-Dimethylaminopyridine and diisopropylethylamine in CH2C12,

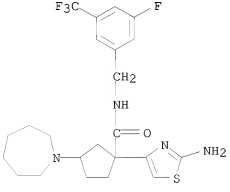
followed by N-deprotection with CF3CO2H and N-acetylation with acetic anhydride to give N-[3-fluoro-5-(trifluoromethyl)benzyl]-3-(azepan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide (II).

IT 835916-80-8P 835916-81-9P 835916-82-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of N-benzylheterocyclylcyclopentanecarboxamide derivs. as modulators of chemokine receptor for treating, ameliorating, controlling, or reducing risk of inflammatory and immunoregulatory disorder or disease)

RN 835916-80-8 CAPLUS
CN Carbamic acid, [4-[1-[[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-3-(hexahydro-1H-azepin-1-yl)cyclopentyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

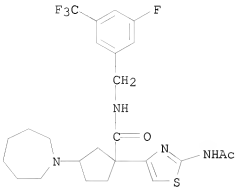


RN 835916-81-9 CAPLUS
CN Cyclopentanecarboxamide, 1-(2-amino-4-thiazolyl)-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX NAME)



RN 835916-82-0 CAPLUS
CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX

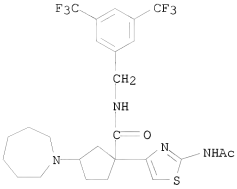
NAME)



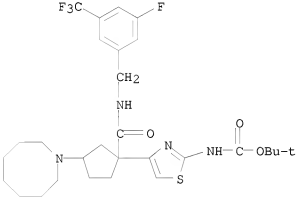
IT 690654-35-4P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azepan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide 835916-83-1P, N-[3-Fluoro-5-(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-[(tert-butoxycarbonyl)amino]thiazol-4-yl]cyclopentane-1-carboxamide 835916-84-2P, N-[3-Fluoro-5-(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-(2-aminothiazol-4-yl)cyclopentane-1-carboxamide 835916-85-3P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-(2-aminothiazol-4-yl)cyclopentane-1-carboxamide 835916-86-4P, N-[3-Fluoro-5-(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide 835916-87-5P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-(acetylamino)thiazol-4-yl]cyclopentane-1-carboxamide 835916-88-6P, N-[3,5-Bis(trifluoromethyl)benzyl]-3-(1-azacyclooctan-1-yl)-1-[2-(pivaloylamino)thiazol-4-yl]cyclopentane-1-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-benzylheterocyclylcyclopentanecarboxamide derivs. as modulators of chemokine receptor for treating, ameliorating, controlling, or reducing risk of inflammatory and immunoregulatory disorder or disease)

RN 690654-35-4 CAPLUS

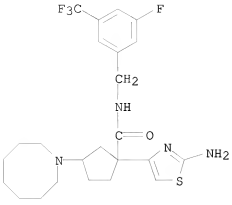
CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX NAME)



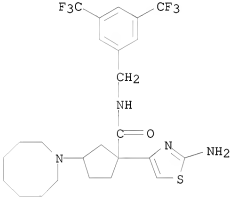
RN 835916-83-1 CAPLUS
CN Carbamic acid, [4-[1-[[[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]amino]carbonyl]-3-(hexahydro-1(2H)-azocinyl)cyclopentyl]-2-thiazolyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



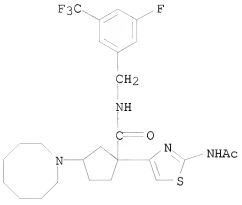
RN 835916-84-2 CAPLUS
CN Cyclopentanecarboxamide, 1-(2-amino-4-thiazolyl)-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)



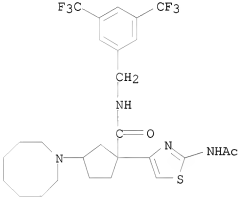
RN 835916-85-3 CAPLUS
CN Cyclopentanecarboxamide, 1-(2-amino-4-thiazolyl)-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)



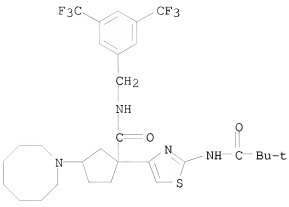
RN 835916-86-4 CAPLUS
CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3-fluoro-5-(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)



RN 835916-87-5 CAPLUS
CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)



RN 835916-88-6 CAPLUS
CN Cyclopentanecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-1-[2-[(2,2-dimethyl-1-oxopropyl)amino]-4-thiazolyl]-3-(hexahydro-1(2H)-azocinyl)- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:412749 CAPLUS
DOCUMENT NUMBER: 140:423705
TITLE: A preparation of piperidinylcyclopentyl amide derivatives, useful as modulators of chemokine receptor activity
INVENTOR(S): Zhou, Changyou; Pasternak, Alexander; Yang, Lihu
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041163	A2	20040521	WO 2003-US34099	20031024
WO 2004041163	A3	20040715		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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CA 2503713	A1	20040521	CA 2003-2503713	20031024
AU 2003284188	A1	20040607	AU 2003-284188	20031024
EP 1558576	A2	20050803	EP 2003-776578	20031024
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US 20060173013	A1	20060803	US 2006-533337	20060330
PRIORITY APPLN. INFO.:			US 2002-422381P	P 20021030
			WO 2003-US34099	W 20031024

OTHER SOURCE(S): MARPAT 140:423705
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

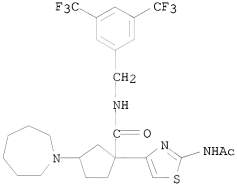
AB The invention relates to piperidinylcyclopentyl amide derivs. of formula I [wherein: X is -O-, -CH2O-, -CO2-, or -OC(O)-, etc.; W is (un)substituted Ph or heterocycle; Z is C, N, or O, wherein when Z is N, then R4 is absent, and when W is O, then both R3 and R4 are absent; n = 0-4; R1 is H, halo, trifluoromethyl, OH, alkyl, or CN, etc.; R2 is (un)substituted C0-6alkyl-(phenyl/heterocycle); R3 is (un)substituted C0-6alkyl-phenyl; R4 is H, OH, CN, or alkyl, etc.; R5 and R6 are independently selected from H, OH, alkyl, alkoxy, or oxo, etc.; R3 and R5 or R4 and R6 may be joined together to form (un)substituted ring] , useful as modulators of chemokine receptor activity. In particular, these compds. are useful as modulators of the chemokine receptor CCR-2. For instance, piperidinylcyclopentyl

amide derivative II (CCR-2 receptor binding IC50 < 1μM) was prepared via amination of the obtained intermediate cyclopentanone derivative III by 4-(4-fluorophenyl)piperidine with a yield of 66% (example 1).

IT 690654-35-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylcyclopentyl amide derivs., useful as modulators of chemokine receptor activity)

RN 690654-35-4 CAPLUS

CN Cyclopentanecarboxamide, 1-[2-(acetylamino)-4-thiazolyl]-N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-3-(hexahydro-1H-azepin-1-yl)- (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT